ACUTE TOXICITY SUMMARY

PROPYLENE OXIDE

(1,2-propylene oxide, methyl ethylene oxide, propene oxide)

CAS Registry Number: 75-56-9

I. Acute Toxicity Summary (for a 1-hour exposure)

Inhalation reference exposure level	**3,100 µg/m³**
Critical effect(s)	dyspnea in mice
Hazard Index target(s)	Eyes; Respiratory System; Reproductive/developmental

II. Physical and Chemical Properties (HSDB, 1994 except as noted)

Description	colorless liquid
Molecular formula	C_3H_6O
Molecular weight	58.08
Density	0.83 g/cm^3 @ 20°C
Boiling point	34.23°C
Melting point	-112.13°C
Vapor pressure	445 mm Hg @ 20°C
Flashpoint	-19.44°C, closed cup
Explosive limits	2.8% - 37%
Solubility	soluble in water, miscible in acetone, benzene, carbon tetrachloride, methanol, ether
Odor threshold	35 ppm (geometric mean) (AIHA, 1989)
Odor description	sweet (AIHA, 1989)
Conversion factor	1 ppm = 2.38 mg/m³ @ 25°C

III. Major Uses or Sources

Propylene oxide is used as a fumigant such as in the sterilization of packaged foods. It is also used as a chemical intermediate in the production of propylene glycol and glycol ethers and as a solvent. Propylene oxide is used in the preparation of surfactants and oil demulsifiers.

IV. Acute Toxicity to Humans

Propylene oxide is a primary irritant of the eyes and of the upper and lower respiratory tracts (HSDB, 1994). Mild CNS depression, indicated by incoordination, ataxia, and depression, are also reported effects of propylene oxide exposure.

In a case-report, an accidental 15-minute human exposure to 1,400-1,500 mg/l (5.9×10^5 - 6.3×10^5 ppm) propylene oxide vapor was reported to result in irritation of the eyes and a burning sensation behind the sternum (Beljaev *et al*., 1971). Late onset symptoms included headache, asthenia, and diarrhea. Recovery was reported to be complete the following day.

Predisposing Conditions for Propylene Oxide Toxicity

Medical: Persons with existing eye, skin, cardiopulmonary, or neurological conditions may be more sensitive to the toxic effects of propylene oxide exposure (Reprotext, 1999).

Chemical: Persons consuming large quantities of foods fumigated with propylene oxide may be more sensitive to toxic effects following inhalation exposure to propylene oxide (Reprotext, 1999).

V. Acute Toxicity to Laboratory Animals

The 4-hour LC_{50}s for mice and rats are reported as 1,740 and 4,000 ppm (4,100 and 9,500 mg/m³) propylene oxide, respectively (Jacobsen *et al*., 1956). The LD_{50} for propylene oxide administered by stomach tube is reported as 1,140 mg/kg in rats and 690 mg/kg in guinea pigs (Smyth *et al*., 1941).

Rats (5 of each sex) were exposed to 1,277, 2,970, 3,794, and 3,900 ppm (3,040, 7,070, 9,030, and 9,300 mg/m³) propylene oxide for 4 hours (NTP, 1985). Dyspnea and red nasal discharge, followed by death, were observed in animals in the three highest exposure groups.

In the same experiment, ten mice (5 of each sex) were exposed to 387, 859, 1,102, 1,277, and 2,970 ppm (920, 2,040, 2,600, 3,040, and 7,070 mg/m³) propylene oxide for 4 hours. Dyspnea was observed in all exposed groups. Narcosis was observed in those mice exposed to 1,102 or 1,277 ppm propylene oxide. Lacrimation was observed in mice exposed to 1,277 ppm propylene oxide. Treatment-related lethality was observed in the three highest exposure groups. While deaths were not observed following exposure to 859 ppm, one female mouse died 6 days following exposure to 387 ppm. The authors suggest that the death observed at 387 ppm was not treatment related. No gross pathologic effects were observed in any of the exposed mice at necropsy.

No studies of the metabolism of propylene oxide were located. Epichlorohydrin, structurally similar to propylene oxide, was found to be readily absorbed in the gastrointestinal and respiratory tracts (USEPA, 1987). By analogy to other structurally similar compounds, propylene oxide is likely to be distributed to the kidneys, liver, pancreas, adrenal glands, and spleen. Glutathione conjugates and carbon dioxide are likely metabolites to be found in the urine and expired air of animals exposed to propylene oxide.

VI. Reproductive or Developmental Toxicity

Female rats exposed to 500 ppm (1,200 mg/m^3) propylene oxide 7 hours per day, 5 days per week for three weeks prior to mating exhibited a significant reduction in the number of corpora lutea, implants, and live fetuses compared to rats exposed from days 7-16 or 1-16 of gestation (Hardin *et al*., 1983). Fetal effects included a significant reduction in fetal body weight and crown-rump length; wavy ribs and reduced skeletal ossification were also noted in propylene oxide exposed litters. Maternal toxicity, indicated by a statistically significant decrease in body weight gain and increased kidney weight, was observed. The same study exposed rabbits in a similar manner to the same concentration; no significant reproductive or developmental effects were observed.

VII. Derivation of Acute Reference Exposure Level and Other Severity Levels (for a 1-hour exposure)

Reference Exposure Level (protective against mild adverse effects): 1.3 ppm (3.1 mg/m^3)

Study	National Toxicology Program, 1985
Study population	10 mice (5 per sex)
Exposure method	inhalation in a chamber
Critical effects	dyspnea (1 death 6 days post exposure)
LOAEL	387 ppm
NOAEL	not observed
Exposure duration	4 hours
Extrapolated 1-hour concentration	774 ppm (387^2ppm * 4 h = C^2 * 1 h) (see Table 12 for information on "n")
LOAEL uncertainty factor	6
Interspecies uncertainty factor	10
Intraspecies uncertainty factor	10
Cumulative uncertainty factor	600
Reference Exposure Level	1.3 ppm (3.1 mg/m^3; 3,100 μg/m^3)

Mice (five of each sex) were exposed to 387 ppm or 859 ppm propylene oxide for 4 hours. Dyspnea was observed in all exposed groups. No gross abnormalities were noted at necropsy. The LOAEL for dyspnea (in this case considered an irritant, mild adverse effect) is 387 ppm propylene oxide. (One female mouse died 6 days following exposure to 387 ppm propylene oxide. Because no deaths were observed in the 859 ppm exposure group, it is plausible that the observed death was not treatment related.)

NTP (1985) reports that propylene oxide acts as an irritant only at the site of administration, the nose in this case. Therefore, the dyspnea reflects nasal irritation, a mild effect. Necropsy findings in the NTP study of animals following both acute and chronic exposures support this assumption.

Level Protective Against Severe Adverse Effects

No recommendation is made due to the limitations of the database.

Level Protective Against Life-threatening Effects

No recommendation is made due to the limitations of the database.

NIOSH (1995) lists a revised IDLH for propylene oxide of 400 ppm based on acute inhalation toxicity/lethality data in mice and dogs. The dog 4-hour LC_{LO} is 2,005 ppm and the mouse 4-hour LC_{50} is 1,740 ppm (Jacobson *et al*. 1956). This value of 400 ppm appears low for a level protective against life-threatening effects based on the case report of complete recovery from a 600,000 ppm exposure for 15 minutes (Beljaev *et al*., 1971).

VIII. References

(AIHA) American Industrial Hygiene Association. Odor thresholds for chemicals with established occupational health standards. Akron (OH): AIHA: 1989. p. 28.

Beljaev VA, Politykin AJ, Cernyseva LA. Acute poisoning by propylene oxide. Gig Prof Zabol 1971;15:48-49. [cited in Gosseline *et al*., 1984.]

Gosseline RE, Smith RP, Hodge HC. Clinical toxicology of commercial products. 5th ed. Baltimore (MD): Williams and Wilkins; 1984.

Hardin BD, Niemeier RW, Sikov MR, Hackett PL. Reproductive-toxicologic assessment of the propylene epoxides ethylene oxide, propylene oxide, butylene oxide, and styrene oxide. Scand J Work Environ Health 1983;9:94-102.

(HSDB) Hazardous Substances Data Bank. National Library of Medicine, Bethesda (MD) (CD-ROM version). Denver (CO): Micromedex, Inc.; 1994. (Edition expires 7/31/94).

Jacobson KH, Hackley EB, Feinsilver L. The toxicity of inhaled ethylene oxide and propylene oxide vapors. AMA Arch Ind Health 1956;13:237-244.

(NTP) National Toxicology Program. NTP Technical report on the toxicology and carcinogenesis studies of propylene oxide in F344/N rats and $B6C3F_1$ mice (inhalation studies). NTP TR 267. Research Triangle Park (NC): US Department of Health and Human Services, Public Health Service, National Institutes of Health; 1985.

Reprotext® System. Dabney BJ, editor. Denver (CO): Micromedex, Inc.; 1994. (Edition expires 7/31/1994).

Reprotext® System. Dabney BJ, editor. Denver (CO): Micromedex, Inc.; 1999. (Edition expires 1/31/1999).

Rowe VK, Hollingsworth RL, Oyen F, McCollister DD, Spencer HC. Toxicity of propylene oxide determined on experimental animals. AMA Arch Ind Health 1956;13:228-236.

Smyth HF Jr, Seaton J, Fischer L. The single dose toxicity of some glycol and derivatives. J Ind Hyg Toxicol 1941;23(6):259-268.

(USEPA) United States Environmental Protection Agency. Summary review of the health effects associated with propylene oxide. Health issue statement. Research Triangle Park (NC): Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, USEPA; 1987.